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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In the application of:

Examiner: Nirmal Singh Basi

Terry P. SNUTCH and David L. Baillie

Group Art Unit: 1646

• Serial No.: 09/030,482

Filing Date: 25 February 1998

For: NOVEL HUMAN CALCIUM  
CHANNELS AND RELATED PROBES,  
CELL LINES AND METHODS

## **BRIEF ON APPEAL**

**Box AF**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Appeal is taken from a final rejection mailed 3 July 2002 of claims 28-33 in the above-referenced case. A Notice of Appeal was filed in this case on 23 August 2002, thus setting a date for filing of the Brief of 23 October 2002. A petition for an extension of time of four (4) months until 23 February 2003 is attached along with the required fee. In accordance with 37 C.F.R. § 1.192, this Brief, along with the Appendix, is filed **in triplicate** and is accompanied by the required fee.

There is no rejection over the art. Two declarations already of record are attached as Exhibits A and B for the convenience of the Board. An article describing the relevance of T-type  $\text{Ca}^{+2}$  channels in cardiac disease: Heady, T., *et al.*, *Jpn. J. Pharmacol.* (2001) 85:339-350, is

sd-128922

attached as Exhibit C. Exhibit D (2 pages) shows schematics of voltage gated  $\text{Ca}^{+2}$  channels. U.S. patent 5,710,250, Exhibit E, shows that claims have been issued on calcium ion channel subunits where markedly less than the full-length sequence of the subunit is disclosed and wherein even the full-length sequence is nonfunctional.

Exhibit F is an article by Klugbauer, Ed, *et al.*, *J. Neurosci.* (1999) 19:684-691 that establishes nonfunctionality of  $\alpha_2$  subunits, the subject of Exhibit E, to perform as calcium ion channels. Also enclosed are U.S. 6,309,858; and U.S. 6,358,706 as Exhibits G and H. The relevance of these exhibits is further explained below.

**1. Real Party in Interest**

The real party in interest is NeuroMed Technologies Inc., of Vancouver, Canada, a Canadian corporation, which is the assignee herein.

**2. Related Appeals and Interferences**

Neither appellants, appellants legal representative nor assignee are aware of any appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**3. Status of Claims**

The application was filed with claims 1-15. Appellants' opted to prosecute the invention of original claims 1-11 and 13-14; claims 12 and 15 were withdrawn from consideration. In response to an initial Office action, all pending claims were canceled and claims 16-33 were substituted. These claims were directed to recombinant materials related to the protein encoded by SEQ. ID. No.: 18, *i.e.*, a human T-type  $\text{Ca}^{+2}$  channel  $\alpha_1$  subunit. An amendment was proposed in response to final rejection which was not entered; however, a Continued Prosecution Application (CPA) was filed on 4 September 2001 requesting entry of this amendment. In that

amendment, which was entered after filing the CPA, claims 16-27 were canceled and claims 28-33 were amended to require that the encoded T-type calcium channel be "functional." In response to an initial Office action, claim 28 was amended to specify that the claimed DNA molecule be "isolated." No further amendment was made to the claims and no response was filed to the final rejection mailed 3 July 2002. Claims 28-33 remain and are on appeal.

**4. Status of Amendments**

No amendments were proposed subsequent to final rejection.

**5. Summary of the Invention**

The claims are directed to recombinant materials for production of the functional subunit ( $\alpha_1$ ) corresponding to a type of calcium ion channel for which the genes were previously unknown. The existence of this type of channel, designated "T-type" or "low-voltage activated" channel, was understood because behavior of this type of channel had been observed, and at least one antagonist specific for this channel had been on the market as a drug for cardiac conditions (see Exhibit C, page 340, right column).

Certain types of calcium ion channels, designated L, N, P and Q are activated at relatively high potentials (page 2, lines 26-27) and nucleotide sequences encoding the subunits of these channels had been obtained in the past (page 4, lines 1-6); the subunits  $\alpha_{1A}$ - $\alpha_{1D}$  and  $\alpha_{1S}$  represent the L, N, or P/Q type channels;  $\alpha_{1E}$  represents a still different type of channel (see Table 1 on page 7). However, the T-type channel, which is activated at lower potential (page 2, lines 24-25) had not been characterized as associated with a particular nucleotide sequence or gene (page 6, lines 1-10). It had long been desired to obtain recombinant materials which would permit the recombinant production of the  $\alpha_1$  subunit of T-type channels because the  $\alpha_1$  subunit alone can

form a functional T-type calcium channel; the function of additional subunits is only to modulate its activity (page 5, lines 16-26).

Although others had attempted to retrieve the nucleotide sequences encoding  $\alpha_1$  subunits of T-type channels using traditional cloning techniques (whereby DNA encoding  $\alpha_1$  subunits of calcium ion channels for which the native nucleotide sequences were known are used to probe cDNA or genomic libraries), there was no success. Appellants took a different approach. Appellants screened the *C. elegans* genomic DNA sequence database for sequences homologous to the previously identified mammalian calcium channel  $\alpha_1$  subunits (page 9, lines 17-19). This resulted in identifying four *C. elegans* cosmids that contained coding regions homologous to these  $\alpha_1$  subunits (page 10, lines 9-14). By phylogeny analysis, two of the cosmids were considered to relate to the  $\alpha_1$  subunits that were already known; two were considered to represent distinct  $\alpha_1$  subunit types (page 10, lines 15-20). Then, screening the EST databank for mammalian counterparts of one of these cosmids showed the presence of sequences that encoded conserved regions just sufficiently similar to the calcium channel nucleotide sequences already known to encode the T-type channel, but not similar enough to encode the high voltage channels (page 11, lines 3-9). By placing these sequences in context of human chromosomes, it was shown that four of the five sequences resided on chromosome 22 and were considered part of the same gene. By applying bioinformatics, the translated sequence of the appropriate region of this chromosome was found to encode the T-type channel  $\alpha_1$  subunit. It is this nucleotide sequence (which encodes T-type channel  $\alpha_1$  subunit) that is SEQ. ID. No.: 18. DNA comprising this nucleotide sequence is the subject of the claims (page 13, lines 15-25).

Although these methods are not claimed in the present application, it was the application of these creative methods that permitted the T-type  $\alpha_1$  subunit encoding sequence to be

recovered. Now that an  $\alpha_1$  T-type encoding nucleotide sequence had been found, it was understood to be useful to construct probes to recover genes encoding T-type channels from other species and any other genes located in the same organism which also encode the T-type channel  $\alpha_1$  subunit. It was recognized that this should be done using conditions of medium hybridization stringency (page 15, line 2) because this stringency would be sufficient to exclude sequences encoding high voltage type  $\text{Ca}^{+2}$  channels. It was further envisioned and claimed that the resulting materials would be cloned into expression vectors and used to produce the calcium ion channel  $\alpha_1$  subunit (page 15, lines 14-15). The expressed sequences, which effect display of the  $\alpha_1$  subunit on the host cells, can then be used to screen for blockers of calcium ion channel activity (page 15, lines 23-27). This is the case because unlike the situation for high voltage activated channels, only the  $\alpha_1$  subunit is required for functionality (page 5, lines 16-26). Such compounds as are thus identified would be useful in treating a multiplicity of conditions such as epilepsy, migraine, ataxia, schizophrenia, hypertension, arrhythmia, angina, depression, small lung carcinoma and Lambert-Eaton syndrome (page 9, lines 7-10).

Thus, SEQ. ID. No.: 18 encodes the  $\alpha_1$  subunit of a T-type channel. The translated protein is shown, and constitutes about 85% of the total amino acid sequence, sufficient to disclose, inherently, the nucleotide sequence encoding a functional channel. The relationship of this length sequence to the required functionality was demonstrated during prosecution and will be discussed further below.

## 6. Issues

There are three issues raised by the Examiner:

1. Does the disclosure of 85% of the amino acid sequence of the  $\alpha_1$  T-type subunit provide a sufficient written description of a functional calcium ion channel and thus of the nucleotide sequence encoding it?
2. Are conditions of “medium hybridization stringency” so indefinite as to fail to comply with 35 U.S.C. § 112, paragraph 2?
3. Is there a disclosed real-world utility for the claimed subject matter?

## 7. Grouping of Claims

The claims may be considered together.

## 8. Argument

Each of the issues set forth above is addressed as follows:

A. The Translation Shown of SEQ. ID. No.: 18 is a Sufficient, Enabling Written Description of a Functional T-Type Calcium Ion Channel and thus of a Nucleotide Sequence Encoding It

First, it is unclear whether the Examiner disputes the statements made in the specification that the  $\alpha_1$  subunit of the T-type channel, displayed alone, provides functional calcium ion channel activity. The application clearly states that calcium ion channel activity is exhibited by the  $\alpha_1$  subunit taken alone. Page 3, lines 19-20, state that the  $\alpha_1$  subunit is the major pore forming subunit and contains a voltage sensor and binding sites for calcium channel antagonists. Page 5, lines 15-17, state that the  $\alpha_1$  subunit alone can form functional calcium channels, which additional subunits may at best modulate. Example 2 (that describes assessing calcium ion channel activity) states that the  $\alpha_1$  calcium channel cDNA may be transfected alone into cells for

performing such assessment as well as in combination (page 18, lines 9-10; page 19, lines 11-12). Appellants have found nothing in the record either of evidence or of reasoning that would cause the reader to doubt these statements. Absent such reasoning or evidence, these statements must be accepted. *In re Marzocchi*, 439 F2d 220, 169 USPQ 367 (CCPA 1971).

Clearly in contention, however, is whether the disclosure of a nucleotide sequence encoding 85% of the full-length channel provides a sufficient description of the functional channel to place this channel in the art, and to convey to the skilled artisan that the appellants were in possession of recombinant materials that encode functional T-type  $\alpha_1$  subunits. Appellants have submitted sworn testimony providing evidence that disclosure of the nucleotide sequence encoding 85% of the full-length  $\alpha_1$  subunit demonstrates possession of recombinant materials for production of a functional calcium ion channel. There is no dispute that if the protein containing only the sequence translated were produced, this would not itself be functional. However, there is no requirement that a written description be set forth *in haec verba* in the application in order to be considered adequate. See, for example, *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F2d 1419, 5 USPQ2d 1194 (Fed. Cir. 1987). In that case, claims to ceramics with an equiaxed structure were considered supported in the parent application which failed to mention this characteristic. The characteristic was considered inherent in the description provided of the material itself.

Similarly, here, the description of the essential portion missing 15% of the amino acid sequence (domain IV) is inherent in the description of the 85% set forth in the application.

It may be helpful to provide some background information on the known structural features of voltage-gated ion channels. A rough illustration of the disposition of these channels in the cell membrane is shown on page 1 of Exhibit D. As shown, the  $\alpha_1$  subunit is the major

feature of the channel which contains the pore-forming unit as well as a voltage sensor. In high voltage channels, the  $\alpha_1$  subunit is associated with a  $\beta$  subunit which is intracellular (the T-type channels lack association with  $\beta$ ) and with an  $\alpha_2\delta$  subunit, a major portion of which is extracellular. A  $\gamma$  subunit may also span the membrane in association with the  $\alpha_1$  subunit.

Exhibit D, page 2, shows a schematic of the  $\alpha_1$  subunit in more detail. Starting at the N-terminus, which is internal to the cell, there are four domains, I-IV, homologous to each other, each of which contains six transmembrane segments, including the illustrated S4.region that acts as a voltage sensor and a P-loop or pore region that contains the amino acid residues responsible for ion selectivity. Domains II and III are separated by a large intracellular loop which has additional functions not relevant here. The 85% of the amino acid sequence set forth in the specification extends past the complete domain III as shown in the figure. The missing portion is only a portion of domain IV.

This was explained under oath by one of the appellants, Dr. Terrance Snutch, who is a recognized practitioner in this field. As Dr. Snutch explains, in paragraph 8 of his declaration (Exhibit A), the explicitly disclosed sequence SEQ. ID. No.: 18 starts at the N-terminus and encodes three complete homologous structural domains, I, II and III up to a transmembrane segment of domain IV that precedes the pore region of domain IV. As Dr. Snutch testified, it is well known that structural domains II, III and IV result from the evolutionary duplication of domain I. (See also Exhibit C, page 339, right column.) Therefore, the remaining sequence in structural domain IV will be functional if it is simply a replication of the already disclosed sequence of domain III. One of ordinary skill would have no difficulty in “filling in the blanks” of the *in haec verba* described sequence since the necessary verbiage is inherent in the 85% of the sequence already disclosed.

Respectfully, to require an *in haec verba* description of sufficient sequence to represent a functional  $\alpha_1$  subunit puts form over substance. The ordinary practitioner would require no experimentation in order to provide a nucleotide sequence encoding a functional calcium ion channel. The nature of the omitted 15% is simply inherent in the description of the 85% described, when put in context of the further description that this represents a calcium ion channel whose evolutionary history is well understood in the art. It would be equivalent to stating that a written description is inadequate if a word is omitted from a sentence when the reader would automatically know that it was there. Is the sentence, "The sun rises the morning" an inadequate non-enabling written description because "in" is missing between "rises" and "the"? There should be 23 letters in the sentence and there are only 21. Therefore, 10% of the letters are missing. But could anyone possibly fail to understand what the other two letters have to be? They are inherent in the sentence as presented.

Appellants further call the attention of the Office to U.S. patent 5,710,250 (Exhibit E). This patent contains claims to a "substantially pure  $\alpha_2$  subunit of a human calcium channel encoded by DNA comprising a sequence of nucleotides that encodes the  $\alpha_2$  subunit of a human calcium channel." The structural characteristics of the coding nucleotide sequence are defined in the claims as the ability to hybridize under conditions of high stringency with a "naturally occurring complementary DNA encoding a human calcium channel subunit" that includes "all or a portion of the nucleotide sequence set forth in Figures 2a-2f and the portion includes at least nucleotides 43-272" of those figures. Figures 2a-2f do not encode a human  $\alpha_2$  subunit, they encode a rat skeletal muscle  $\alpha_2$  subunit. The actual nucleotide sequence encoding a human  $\alpha_2$  subunit is set forth in Figures 3a-3d and is marvelously incomplete. It comprises only 1,849 nucleotides out of an expected 7,000-8,000.

The claims of this patent are presumed valid under 35 U.S.C. § 282, so appellants are entitled to assume that a claim to a “functional”  $\alpha_2$  subunit of a calcium ion channel can validly issue based on the disclosure as a written description of the actual human nucleotide sequence corresponding to less than half of its full-length, a proportion that is clearly not itself functional. If that assumption is true, then it seems more than reasonable that a description *in haec verba* of 85% of the relevant full-length sequence would be adequate to support a claim to recombinant materials encoding a functional channel.

Furthermore, even the full-length  $\alpha_2$  subunit claimed in the ‘250 patent, taken alone, is not “functional” - there is no description in the ‘195 patent which even asserts functionality of the  $\alpha_2$  subunit taken alone; indeed, it is now known that the  $\alpha_2$  subunit is actually associated with further amino acid sequence and comprises an  $\alpha_2\delta$  subunit as shown on page 1 of Exhibit D. As described in Exhibit F, the  $\alpha_2\delta$  subunit does not function alone, but rather modulates the calcium ion channel activity of the  $\alpha_1$  subunit. As stated, for example, in the Abstract, “Coexpression of  $\alpha_2\delta$ -3 with  $\alpha_{1C}$  and cardiac  $\beta_{2A}$  or  $\alpha_{1E}$  and  $\beta_3$  subunits shifted the voltage dependence of the channel activation and inactivation in a hyperpolarizing direction and accelerated the kinetics of current inactivation. There is no description of  $\alpha_2\delta$  subunits functioning alone; they require the presence of  $\alpha_1$  in order to function.

For the reasons set forth above, appellants request that the Board recognize that an adequate written description of the claimed subject matter has been provided.

B. “Medium Hybridization Stringency” is Sufficiently Definite to Comply with the Statute

The Examiner objects that without specific hybridization conditions being set forth in the application, one of ordinary skill would not be able to define the metes and bounds of the claims

by reference to "medium hybridization stringency." Appellants, however, believe that in light of the testimony of record, the statutory requirements are met. To meet the statutory requirements, it is sufficient if the claim language is such that a person of ordinary skill can discern how to avoid infringement (*Morton International, Inc. v. Cardinal Chemical Company*, 5 F3d 1464, 28 USPQ2d 1190 (Fed. Cir. 1993)). The claim as presented does this.

"Medium hybridization stringency" defines a narrow range of sequence homology (see paragraph 4 of Dr. Snutch's declaration submitted October 10, 2000, Exhibit B). This range is sufficiently definite that clearly one could discern how to avoid infringement. As stated in Dr. Snutch's declaration, it is understood that it is the wash conditions that determine the ultimate stringency of the hybridization; these conditions for medium stringency are known in the art to range from 0.1%-0.3% SDS, 2 x SSPE-0.2 x SSPE and 55°C-65°C. These conditions represent a homology of at least 70%. The reader would first understand that this range is intended to cover alternative nucleotide sequences that encode T-type channel  $\alpha_1$  subunits of other species and similar types of subunits residing in other genes of the same species, as stated in the specification on page 15, lines 1-3, and would be such that high voltage activated channel-encoding DNA would be excluded. As stated by the Court in *Morton International*, citing *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986), "Whether a claim is invalid for indefiniteness requires a determination whether those skilled in the art would understand what is claimed when the claim is read in light of the specification." Clearly that is the case here.

More important, it should be apparent that there is nothing inherently uncertain or indefinite about claiming a range as opposed to a single value for a parameter. There is a multiplicity of patents issued with claims with percentage ranges in compositions, for example.

Dr. Snutch has testified that the skilled artisan would recognize that "medium stringency" represents a specific range of stringencies and therefore a specific range of homology. There has been no evidence of record to contradict Dr. Snutch's testimony. If an accused polynucleotide binds to the nucleotide sequence encoding the amino acid sequence encoded by SEQ. ID. No.: 18 (which is admittedly definite) at any of the conditions within the range set forth in Dr. Snutch's declaration, it clearly falls within the scope of the claim. Anyone could readily determine whether a particular nucleic acid would infringe. The Office provides no reason to assert that conditions of hybridization must be set at a single value rather than at a range.

It will be noted that in instances where claims have been considered indefinite by virtue of a range, the metes and bounds of the range could not be ascertained. Thus, in *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F2d 1200, 1218, 18 USPQ2d 1016 (Fed. Cir. 1991) cert. denied, 502 U.S. 856 (1991), Genetics Institute's claims to erythropoietin with a specific activity of "at least about 160,000" were considered invalid, not because a range of specific activities was set forth in the claim, but because the metes and bounds of the range could not be ascertained from either the claim itself or from the record. In the present instance, there is a declaration of record, uncontroverted, which sets forth the understanding in the art of specific metes and bounds of medium stringency.

Accordingly, the ordinary artisan would understand the scope of the claims with sufficient clarity to avoid infringement.

Again, attention of the Office is called to U.S. patent 5,710,250 (Exhibit E), the claims of which are presumed valid. Claim 1 of that application defines the structural characteristics of the claimed nucleotide sequence in terms of hybridization at "high stringency." "High stringency" is nowhere defined in the specification in terms of any wash conditions or any conditions at all.

Evidently, such an art-known description is considered adequate to result in a putatively valid claim.

For the foregoing reasons, appellants respectfully request that the Board reverse the rejection under 35 U.S.C. § 112, paragraph 2.

C. The Utility of the Claimed Subject Matter is Established

The specification clearly describes utility of the recombinant materials claimed. It is to provide recombinant  $\alpha_1$  subunits which can be used in an assay system to identify compounds which would be useful in treating specifically enumerated diseases including epilepsy, migraine, ataxia, schizophrenia, hypertension, arrhythmia, angina, depression, small lung carcinoma and Lambert-Eaton Syndrome. (See page 9, lines 7-10.) The Examiner has failed to provide a *prima facie* case that the utility described is not specific (the utility relies on the specific nexus between the T-type calcium channel and the conditions) or substantial (the conditions listed are certainly substantial) or not credible (there is no reason to believe that the compounds identified will not be useful for further development in obtaining pharmaceuticals to treat these conditions).

Absolute certainty that identified compounds will be thus successful is not required.

*In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995).

There is no reasoning or evidence presented on the record for doubting appellants' characterization of the utility or to provide a *prima facie* case that the utility is insubstantial or non-specific or not credible. The Examiner has simply asserted without basis that the asserted utility does not meet the required criteria.

Appellants request judicial notice be taken of U.S. patents 6,309,858 and 6,358,706 (Exhibits G and H), also presumed valid. The utilities of  $\alpha_1$  subunits of T-type calcium channels are described in substantially the same way in the specifications of these patents as the

description herein. In the '706 patent, at column 16, beginning at line 11, the same approach as described herein is set forth. The nature of the diseases that can be treated by the compounds identified are set forth in column 17, beginning at line 17. It is not seen that the nature of the description in the '706 patent differs materially from that herein. Similarly, in the '858 patent, the  $\alpha_1$  subunit is used to screen for modulators as set forth in column 2, lines 53-63 and column 18, line 17-column 19, line 63. The use of the compounds identified is set forth in a manner similar to that set forth in the present specification in column 19, lines 63-66.

In addition, Exhibit C clearly establishes that compounds that are selective for T-type channels would be useful pharmacologically. For example, on page 347, it is stated

Although to date there are no highly selective T-type channel blockers, studies using a variety of compounds that all have activity against these channels have led to the conclusion that selective blockers might be useful in regulating proliferation, blood pressure and abnormal neuron firing. T-type channels may play a central role in thalamic dysrhythmias and therefore blockers may be useful not only against epilepsy, but also a wide spectrum of neurological disorders.

It is precisely for the purpose of discovering such selective T-type blockers that the claimed materials are useful. No reason can be comprehended by appellants as to why their descriptions of utility are considered inadequate. Accordingly, reversal of the rejection grounded in lack of utility is respectfully requested.

## 9. Appendix

An Appendix containing a copy of the claims involved in the appeal is attached.

## CONCLUSION

Appellants have shown that the description in the application of a nucleotide sequence encoding 85% of the full-length  $\alpha_1$  subunit of the T-type receptor inherently describes the

relevant portion of the remaining 15% and thus adequately describes a sequence encoding a functional  $\alpha_1$  subunit. Further, one of ordinary skill would understand the meaning of "medium hybridization conditions" sufficiently to avoid infringement of the claims. In addition, appellants have described a conventional specific, substantial, and credible utility for the recombinant materials claimed. Appellants respectfully request that the rejections set forth by the Examiner be reversed and claims 28-33 be passed to issue.

The Assistant Commissioner is hereby authorized to charge any additional fees under 37 C.F.R. § 1.17 that may be required by this Brief, or to credit any overpayment, to Deposit Account No. 03-1952.

Respectfully submitted,

Dated: February 24, 2003

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## APPENDIX

28. An isolated DNA molecule which comprises an expression system for the production of a calcium ion channel  $\alpha_1$  subunit protein which expression system comprises a nucleotide sequence encoding a functional T-type, low voltage activated calcium channel  $\alpha_1$  subunit or the complement to said encoding nucleotide sequence, wherein said encoding nucleotide sequence comprises

- (a) a nucleotide sequence encoding the amino acid sequence encoded by SEQ. ID. NO: 18; or
- (b) the complement of a nucleotide sequence that hybridizes under conditions of medium hybridization stringency to the nucleotide sequence of (a).

29. The DNA molecule of claim 28 wherein said encoding nucleotide sequence encodes the amino acid sequence encoded by SEQ. ID. NO: 18.

30. The DNA molecule of claim 29 wherein said encoding nucleotide sequence is that set forth in SEQ. ID. NO: 18.

31. Recombinant host cells which are modified to contain the DNA molecule of any of claims 28-30.

32. A method to produce a functional T-type calcium ion channel  $\alpha_1$  subunit protein which method comprises culturing the cells of claim 31 under conditions wherein said expression system produces said protein.

33. A method to prepare cells which produce a functional T-type calcium ion channel  $\alpha_1$  subunit protein which method comprises introducing into said cells the DNA molecule of claim 28.

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Docket No.: 381092000700	Atty: Kate H. Murashige
Serial No.: 09/030,482	Filing Date: 25 February 1998
Title: NOVEL HUMAN CALCIUM CHANNELS AND RELATED PROBES, CELL LINES AND METHODS	
Date of Mailing: February 24, 2003 via First Class Mail	

Papers enclosed herewith:

1. Transmittal Form (1 page)
2. Fee Transmittal (1 page, 1 duplicate)
3. Petition for Extension of Time (2 pages, 1 duplicate)
4. Brief on Appeal (16 pages)
5. Exhibits A-H
6. Return Postcard

All submitted in Triplicate

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